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Applicants:	Hanson, R.N. et al.	Atty. Docket No.:	ZAA-011.01
Serial No.:	09/758,957	Examiner:	Garcia, M.E.
Filing Date:	11 January 2001		
Title:	<i>Polypharmacophoric Agents</i>	Art Unit:	1627

Assistant Commissioner for Patents  
Washington, DC 20231

**Certificate of Mailing**

I hereby certify that this "Notification of Defective Restriction Requirement" is being deposited with the U. S. Postal Service as First Class Mail with sufficient postage on the date set forth below in an envelope addressed to:  
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4/9/02

By: Terrill Williams  
Terrill Williams

Date of Signature and Mail Deposit

***Notification of Defective Restriction Requirement***

Dear Examiner Garcia:

In response to the Restriction Requirement in the above-identified application, mailed March 21, 2002, the Applicants respectfully notify the Examiner that the Restriction Requirement is defective. Specifically, while the cover page (Form PTO-90C) corresponds to the above-identified application, the Office Action Summary and the substance of the Restriction Requirement correspond to USSN 09/718,975. The original Restriction Requirement accompanies this paper. The Applicants respectfully request that the Examiner issue a corrected Restriction Requirement in the above-identified application, resetting the mailing date and the various deadlines for reply.

The Applicants believe that no fees are due in connection with the filing of this Response. Nevertheless, the Commissioner is hereby authorized to charge to our Deposit Account, **No. 06-1448**, any fees due in connection with the filing of this Response.

Respectfully submitted,  
Foley, Hoag & Eliot LLP

By: Dana Gordon

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Date: 4/9/02

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/758,957	01/11/2001	Robert N. Hanson	ZAA-011.01	9648

25181 7590 03/21/2002

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*Restriction Requirement*  
**DUE:** 4-21-02  
**FINAL:** 9-21-02

EXAMINER

GARCIA, MAURIE E

ART UNIT

PAPER NUMBER

1627

DATE MAILED: 03/21/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

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**Office Action Summary**PATENT &  
TRADEApplication No.  
09/718,975

Applicant(s)

Affholter et al

Examiner

Padmashri Ponnaluri

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1)  Responsive to communication(s) filed on Nov 22, 2000
- 2a)  This action is FINAL.      2b)  This action is non-final.
- 3)  Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

**Disposition of Claims**

- 4)  Claim(s) 1-141 is/are pending in the application.
- 4a) Of the above, claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5)  Claim(s) \_\_\_\_\_ is/are allowed.
- 6)  Claim(s) \_\_\_\_\_ is/are rejected.
- 7)  Claim(s) \_\_\_\_\_ is/are objected to.
- 8)  Claims 1-141 are subject to restriction and/or election requirement.

**Application Papers**

- 9)  The specification is objected to by the Examiner.
- 10)  The drawing(s) filed on \_\_\_\_\_ is/are objected to by the Examiner.
- 11)  The proposed drawing correction filed on \_\_\_\_\_ is: a)  approved b)  disapproved.
- 12)  The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. § 119**

- 13)  Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a)  All b)  Some\* c)  None of:

1.  Certified copies of the priority documents have been received.
2.  Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3.  Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\*See the attached detailed Office action for a list of the certified copies not received.

- 14)  Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

**Attachment(s)**

- 15)  Notice of References Cited (PTO-892)
- 16)  Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 17)  Information Disclosure Statement(s) (PTO-1449) Paper No(s). \_\_\_\_\_
- 18)  Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 19)  Notice of Informal Patent Application (PTO-152)
- 20)  Other: \_\_\_\_\_

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Application/Control Number: 09/718,975

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**DETAILED ACTION**

1. The preliminary amendment A, filed on 11/22/00 has been fully considered and entered into the application.
2. Claims 1-141 are currently pending in this application.

***Election/Restriction***

3. Restriction to one of the following inventions is required under 35 U.S.C. 121:

- I. Claims 1-15, 19-26, drawn to a method of obtaining a polynucleotide that encodes an improved polypeptide comprising monooxygenase activity, classified in class 435, subclass 4.
- II. Claims 16-17, drawn to a library of recombinant polynucleotide, classified in class 536, subclass 23.1.
- III. Claims 18 and 27, drawn to an improved monooxygenase encoding nucleic acid, classified in class 536, subclass 23.2.
- IV. Claims 28-29, drawn to a DNA shuffling mixture, classified in class 536, subclass 23.1.

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- V. Claims 30-33, drawn to a method for increasing monooxygenase activity in a cell, classified in class 435, subclass 41+.
- VI. Claims 34-37, drawn to a method for obtaining a polynucleotide encoding an improved polypeptide acting on a substrate, classified in class 435, subclass 6.
- VII. Claims 38-43, drawn to a polypeptide encoded by a polynucleotide, classified in class 530, subclass 300+.
- VIII. Claims 44-45, drawn to a method of oxidizing a substrate, classified in class 530, subclass 333 or class 435, subclass 68.1.
- IX. Claims 46, drawn to a method for preparing a hydroxy methyl group, classified in class 435, subclass 68.1.
- X. Claim 47, drawn to a method for preparing an epoxide group, classified in class 435, subclass 68.1.
- XI. Claim 48, drawn to a method for preparing a hydroxy methylene group, classified in class 435, subclass 68.1.
- XII. Claim 49, drawn to a method for preparing a hydroxyaryl group, classified in class 435, subclass 68.1.

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- XIII. Claims 50 (in part), 51-52, drawn to an organism comprising a recombinant monooxygenase polynucleotide and an improved transferase polypeptide, classified in class 435, subclass 193.
- XIV. Claims 50 (in part), 53-54, drawn to an organism comprising a recombinant monooxygenase polynucleotide and an improved ligase peptide , classified in class 435, subclass 193.
- XV. Claims 50 (in part), 55-56, drawn to an organism comprising a recombinant monooxygenase polynucleotide and an improved racemase polypeptide, classified in class 435, subclass 193.
- XVI. Claims 50 (in part), 57-58, drawn to an organism comprising a recombinant monooxygenase polynucleotide and dehydrogenase polypeptide, classified in class 435, subclass 193.
- XVII. Claims 50 (in part), 59-61, drawn to an organism comprising a recombinant monooxygenase polynucleotide and an improved solvent resistance polypeptide, classified in class 435, subclass 193.

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- XVIII. Claims 50 (in part), 62-63, drawn to an organism comprising a recombinant monooxygenase polynucleotide and an epoxide hydrolase polypeptide, classified in class 435, subclass 193.
- XIX. Claims 50 (in part), 64, drawn to an organism comprising a recombinant monooxygenase polynucleotide and further comprises two or more recombinant polynucleotides, classified in class 435, subclass 193.
- XX. Claims 65-66, drawn to a method for preparing an epoxide group, classified in class 435, subclass 41+.
- XXI. Claims 67-74, drawn to a method for converting an olefin into a vicinal diol, classified in class 435, subclass 41+.
- XXII. Claims 75-87, drawn to a method for converting an olefin into an alpha-hydroxy carboxylic acid, classified in class 435, subclass 41+.
- XXIII. Claims 88-106, drawn to a method for preparing a hydroxyl group, classified in class 435, subclass 41+.

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XXIV        Claims 107-109, drawn to a method for preparing a hydroxy methylene group, classified in class 435, subclass 41+.

XXV.        Claims 110-117, drawn to a method for preparing a hydroxyaryl group, classified in class 435 subclass 41+.

XXVI.       Claim 118, drawn to a screening process, classified in class 435, subclass 4.

XXVII.      Claims 119-123, drawn to a bioreactor, classified in class 435, subclass 289.1.

XXVIII.     Claims 124-125, drawn to a kit comprising at least one improved monooxygenase polypeptide, classified in class 435, subclass 810.

XXIX.       Claims 126-128, drawn to a recombinant P450 polypeptide, classified in class 935, subclass 11.

XXX.        Claim 129, drawn to a polynucleotide that encodes a recombinant P450 polypeptide, classified in class 935, subclass 10.

XXXI.       Claims 130-133, drawn to a method of obtaining a polynucleotide that encodes a recombinant P450 polypeptide comprising a backbone domain and an active site domain, classified in class 435, subclass 69.1.

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XXXII. Claims 134-137, drawn to a method of obtaining a polynucleotide that encodes a recombinant P450 polypeptide comprising a backbone domain and an active site domain, classified in class 435, subclass 69.1.

XXXIII. Claims 138-141, drawn to a method of obtaining a polynucleotide that encodes a recombinant P450 polypeptide comprising a backbone domain and an active site domain, classified in class 435, subclass 69.1.

4. The inventions are distinct, each from the other because of the following reasons:

Inventions groups 1-33 are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are drawn to different methods, or organisms or compositions or recombinant polypeptides or polynucleotides encoding the polypeptides, which are structurally and functionally different and each group does not require the other for practice .

5. Inventions of groups I, V, VI, VIII, IX-XII, XX-XXVI, XXXI-XXXIII are drawn to different methods. The different methods have different method steps

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and the reagents used are different and effects of the methods are different, and the methods are not used together.

6. Inventions of groups II-IV, VII, XIII-XIX, XXVIII-XXIX are drawn to different products. The different products are structurally and functionally different from each other and are not used together.

7. Inventions of group II, III (products) and group I are related as process of making and product made. The inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make other and materially different product or (2) that the product as claimed can be made by another and materially different process (MPEP § 806.05(f)). In the instant case different products can be made using the group I methods. Thus restriction is proper..

8. Inventions of group XIII and groups XX-XV are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)).

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In the instant case the product can be used in several different processes, thus restriction between the groups is proper.

9. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification and because of their recognized divergent subject matter, restriction for examination purposes as indicated is proper.

Even though some of the groups are classified in the same class/subclass, this has no effect on the non-patent literature search. Different ..... would require completely different searches in non-patent databases, and there is no exception that the searches would be co-extensive. Therefore, these do not create an undo search burden, and restriction for examination purposes as indicated is proper.

10. This application contains claims directed to the following patentably distinct species of the claimed invention:

A) If group I is elected applicants are requested to elect a single species from each of the following:

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- a) applicants are requested to elect one type of monooxygenase activity from claim 3.
  - b) applicants are requested to elect a single species of parental monooxygenase polypeptide of claim 7.
  - c) applicants are requested to elect a single species of library of recombinant polynucleotides from claim 10, 11, 12, 13 and 14.
  - d) applicants are requested to elect a single type of DNA shuffling: family gene shuffling or individual gene shuffling.
  - e) If applicants elect 'library of recombinant transferase' in © supra, applicants are further requested to elect one type of transferase
  - f) Applicants are requested to elect one species of library monooxygenase activity in claim 15.
  - g) applicants are requested to elect a single species of cells in claim 20.
- B) If group II is elected applicants are requested to elect one type of monooxygenase activity.
- C) If group III is elected applicants are requested to elect one type of monooxygenase activity.

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- D) If group V is elected applicants are requested to elect one type of monooxygenase activity.
- E) If group VI is elected applicants are requested to elect a single species of target.
- F) If group VII is elected applicants are requested to elect a single type of polypeptide activity from claim 39, claim 40, claim 41, claim 42.
- G) If group VIII is elected applicants are requested to elect a single species of target from claim 44.
- H) If group XIII is elected applicants are requested to elect a single species of transferase from claim 52.
- I) If group XVI is elected, applicants are requested to elect a single species of groups representing  $R^{11}$ ,  $R^{12}$ ,  $R^{13}$ ,  $R^{14}$ ; and an integer for n, s, p and t.
- J) if group XIX is elected applicants are requested to elect single species of recombinant polynucleotides.
- K) If group XX is elected applicants are requested to elect a single species of substrate from claim 66.

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K) If group XXI is elected applicants are requested to elect a single species representing  $R^1$ ;  $R^2$ ,  $R^3$ , and a single species representing  $R^4$ , of vicinal diol structure in claim 73 and in claim 74.

L) If group XXII is elected applicants are requested to elect

(a) single type of polypeptide activity from claim 79, and in claim 81.

(b) a single species representing  $R^1$ ;  $R^2$ ,  $R^3$ , and single species representing  $R^4$ , of  $\alpha$ -hydroxycarboxylic acid structure of claim 82, claim 83.

© a single species representing  $R^1$ ,  $R^2$ ,  $R^3$ ,  $R^7$ ,  $R^8$ ,  $R^4$ , and a single species representing  $R^5$ , of  $\alpha$ -hydroxycarboxylic acid structure in claim 86.

d) a single species of transferase.

M) if group XXIII is elected applicants are requested to elect a single species of component in claim 96.

N) if group XXIV is elected applicants are requested to elect a single species of substrate in claim 109.

Each of the species are distinct from each other because they are structurally and functionally different from each other and do not require the other for ultimate use, the species election for examination purposes as indicated is proper.

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Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claims 1-2, 4-6, 8-9, 13, 16-24, 27-32, 35-38, 43-45, 50, 118-141 are generic.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is

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the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

11. Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

12. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(I).

13. Applicant is required to reply to this restriction requirement within 30 days of mailing this action. See MPEP 809.2(a).

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**Please Note:** In an effort to enhance communication with our customers and reduce processing time, a dedicated Fax machine is in place to receive your responses. The Fax number is 703-308-4315. A Fax cover sheet is attached to this Office Action for your convenience. We encourage your participation in this Pilot program. If you have any questions or suggestions please contact Jyothsna Venkat, Ph.D., Supervisory Patent Examiner at [jyothsna.venkat@uspto.gov](mailto:jyothsna.venkat@uspto.gov) or 703-308-2439. Thank you in advance for allowing us to enhance our customer service. Please limit the use of this dedicated Fax number to responses to Written Restrictions.

Any inquiry concerning this communication should be directed to P. Ponnaluri whose telephone number is (703) 305-3884. The examiner can normally be reached on Monday through Friday from 8:00 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jyothsna Venkat, can be reached at (703)308-2439. The fax number for this group is (703)305-3014.

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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the group receptionist whose telephone number is (703)308-0196.

P. Ponnaluri  
Patent Examiner  
Technology center 1600  
Art Unit 1627  
16 March 2002



PADMASHRI PONNALURI  
PRIMARY EXAMINER



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ART UNIT: **1627**

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